(1) ***Real Party in Interest***

The real party in interest of the present application is Nektar Therapeutics (formerly Inhale Therapeutic Systems, Inc.), having a place of business at 150 Industrial Road; San Carlos, California 94707.

(2) ***Related Appeals and Interferences***

Appellant, Appellant's legal representative, and assignee are aware of no appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the present appeal.

(3) ***Status of Claims***

Claims 40-59 are presently pending in the case. Claims 40-59 have been finally rejected by the Examiner. The rejections of each of these claims are appealed.

(4) ***Status of Amendments***

No amendments after final have been filed. Applicant's amendment filed on April 16, 2004 has been entered.

(5) ***Summary of claimed subject matter***

The present invention is directed to an inhaleable, spray dried powder formulation comprising a polyene antifungal agent, such as Amphotericin B. Polyenes possess very low solubilities in water and in conventional organic solvents. Thus, formulation of these compounds outside of dry mixing is extremely difficult. The solubility of the polyene can be increased under extreme conditions of pH. However, such conditions typically lead to significant levels of degradation of drug and are usually considered undesirable for the formation of powders for direct administration to the lung.

The present inventors were faced with the challenge of trying to find conditions for spray drying the highly insoluble drug, such as amphotericin B, that (i) did not promote high levels of degradation of drug, (ii) were economically practical, and (iii) resulted in the formation of aerosolizable particles suitable for inhalation.

The presently described and claimed invention relates to the result of this effort. Described are methods for spray drying polyene antifungal agents that result in the formation of chemically stable yet highly dispersible powders. That is to say, the antifungal powders of the invention have excellent aerosol characteristics, such that they are reproducibly prepared and can be efficiently administered by inhalation to the lung, while exhibiting good chemical and physical stability.

In one aspect, the present invention provides a method for preparing a spray dried polyene for oral administration to the lung. The method includes the steps of dissolving a polyene antifungal agent in an acidified solvent and spray drying the polyene solution to form an inhaleable powder containing no more than about 10% polyene degradation products and characterized by an emitted dose of greater than 60%.

In another aspect, a method is provided for preparing a spray dried polyene powder for oral inhalation to the lung in which a polyene antifungal compound is suspended in an aqueous solvent to form a suspension, which is then wet milled, and spray dried. The resulting inhaleable powder contains no more than about 10% polyene degradation products (and typically less than that) and is characterized by an emitted dose greater than about 60%.

(6) ***Grounds of Rejection to be Reviewed on Appeal***

Appellant requests review of the Examiner's following grounds of rejection:

(i) Claims 40 and 42-59 have been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,965,156 to Proffitt et al (hereinafter Proffit et al), in view of PCT Publication WO 97/03649 to Staniforth et al (hereinafter Staniforth et al) and U.S. Patent 6,077,543 to Gordon et al (hereinafter Gordon et al); and

(ii) Claim 41 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Proffitt et al, in view of Staniforth et al, Gordon et al, and further in view of U.S. Patent 4,016,254 to Seager (hereinafter Seager). [Note that it is believed that the Examiner intended to reject claim 41 under these grounds rather than claim 42 as typed in the Final Office Action.]

(7) *Argument*

Appellant believes each of claims 40-59 to be improperly rejected and to therefore be allowable for the at least the following reasons.

The Examiner improperly rejected independent claim 40 under 35 USC 103(a) as being unpatentable over Proffitt et al in view of Staniforth et al and Gordon et al. Claim 40 is to a dry powder for delivery by inhalation to the lungs, the dry powder produced by a method comprising: (i) dissolving a polyene antifungal compound in an acidified solvent to form an acidic polyene-containing solution, and (ii) spray drying said polyene-containing solution to form an inhaleable dry powder containing no more than about 10% polyene degradation products and characterized by an emitted dose greater than 60%. As discussed below, Proffitt et al does not disclose or suggest the powder as claimed. In addition, the teachings of Staniforth et al and Gordon et al would not suggest a modification of Proffitt et al that arrives at the presently claimed invention. Thus, the invention of claim 40 would not have been obvious to one having ordinary skill in the art at the time the invention was made.

Proffitt et al does not render claim 40 unpatentable singly or in combination. Claim 40 is directed to a dry powder for delivery by inhalation to the lungs. In contrast, Proffitt et al discloses a liposomal polyene formulation that is dried and then re-hydrated so that it may be delivered intraveneously to treat systemic fungal infections (see column 4 lines 20-54). Thus, Proffitt et al is not a dry powder for delivery by inhalation to the lungs. The fact that the Proffitt et al powder is dried at one time during its processing does not make it "a dry powder for delivery by inhalation to the lungs". For a dry powder to be deliverable to the lungs it can not be a powder that is prone to hydration. Hydration during storage and/or during delivery in a humid environment will change the aerodynamic character of the powder and will limit the effectiveness of the active agent reaching the lungs. A powder such as the powder of Proffitt et al which is specifically designed to re-hydrate and not specifically designed for inhalation delivery would not be suitable for inhalation delivery. Furthermore, claim 40 recites that the emitted dose, i.e. the dose as defined on page 9 of Appellant's specification, is at least 60%. The presumption by the Examiner that the Proffitt et al powder which is not designed for inhalation delivery would have an emitted dose of at least 60% is, at best, speculative.

In addition, one of ordinary skill in the art would not have found it obvious to modify Proffitt et al in view of Staniforth et al and Gordon et al to change Proffitt et al's

formulation to one that is a powder that is delivered to the lungs because doing so would go against the teachings of Proffitt et al. Proffitt et al is concerned with (1) a manner of making an injectable polyene formulation on a large scale and (2) the treatment of systemic fungal infections. Both of these teachings would be destroyed by the Examiner's proposed modification. Accordingly, not only is there no motivation for one of ordinary skill in the art to make the proposed modification to Proffitt et al, but the person of ordinary skill would be taught away from doing so in that it would destroy the entire purpose of the primary reference. For at least these reasons, Applicant requests withdrawal of the rejection of claim 40.

Claim 41 is also not rendered unpatentable by Proffitt et al. Claim 41 is to a dry powder made by a process comprising, inter alia, suspending a polyene antifungal compound in an aqueous solvent to form a suspension and spray drying the suspension. Proffitt et al teaches a polyene solution and does not teach a polyene suspension that is spray dried. The teachings of Staniforth et al, Gordon et al, and Seager et al do not make up for the deficiencies of Proffitt, and one of ordinary skill in the art would not have found it obvious to modify the process of Proffitt et al based on these teachings, particularly in the absence of motivation to do so.

Independent claims 42, 57 and 58 are not rendered unpatentable by the applied references, either. Claims 42, 57 and 58 are to powder compositions suitable for oral inhalation to the lung comprising a therapeutically effective amount of a polyene antifungal compound. As discussed above, Proffitt et al does not disclose an inhaleable formulation and teaches away from a modification that would result in an inhaleable formulation. Therefore, claims 42, 57, and 58 and claims 43-56 depending from claim 42 are not rendered unpatentable by Proffitt et al, Staniforth et al, and Gordon et al.

For at least these reasons, Appellant requests that the rejection of claims 40-59 be overturned and requests an indication of the allowability thereof.

(8), (9), (10) ***Appendices on following pages***

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ENCLOSURES *(Check all that apply)*

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- [ ] After Final
- [ ] Affidavits/declaration(s)
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Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

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Signature	Guy V Tucker		
Printed name	GUY V. TUCKER		
Date	07 July 2006	Reg. No.	45,302

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